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USE OF A MIXTURE COMPRISING MN(II) AND/OR ZN(II) WITH A BICARBONATE AND AT LEAST AN ORTHO-DIPHENOL, AS AN AGENT REDUCING THE ADHESION OF MICROORGANISMS

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//insert English abstract//

The invention relates to the use of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol in or for the preparation of a

composition, as agent for reducing adhesion of microorganisms, particularly bacteria, on the skin and/or the mucosal membranes. In particular, the compositions of the invention are intended to promote the elimination of bad body odors or to fight against all the skin infections which involve microorganisms, such as, for example, acne and/or dandruff.

It is well known that the skin is covered with a flora which is responsible for a series of annoyances ranging from the simple production of odor to pathologies of varying severities such as, for example, acne and/or dandruff.

The commensal microorganisms which live on or in the skin can either be part of a resident (normal) or transient microflora. The resident microorganisms grow normally on or in the skin. Their presence is established in well defined distribution profiles. The microorganisms which are present temporarily are called transients. Usually, these organisms do not become firmly fixed; they are incapable of multiplying and normally die after a few hours.

The anatomy and the physiology of the skin vary from one part of the body to another part, and the resident microflora reflects these variations.

Most of the bacteria of the skin are present on the superficial squamous epidermis, colonizing the dead cells or the cells which are closely associated with the sebaceous and sudoriparous glands. The excretion of these glands provide water, amino acids, urea, electrolytes and specific fatty acids which serve as nutrients primarily for *Staphylococcus epidermidis* and aerobic corynebacteria.

The Gram-negative bacteria are generally present in the more moist regions.

The yeasts *Pityrosporum ovale* and *Pityrosporum orbiculare* are normally present on the epicranium.

Some dermatophytic mycetes can colonize the skin and cause mycoses, such as, for example, athlete's foot and tinea of the scalp.

Some pathogenic agents which are present on or in the skin are transient residents colonizing the zones around orifices. *Staphylococcus aureus* is the best example. It is present in the nostrils and the perianal region, but survives poorly elsewhere. In the same manner, *Clostridium perfringens* usually colonizes the perineum and the thighs, particularly in patients suffering from diabetes.

Theoretically, the epidermis is not an environment favorable to the colonization by microorganisms. Several factors, such as periodic drying of the skin, the slightly acidic pH of the skin, the high concentration of sodium chloride of sweat, some natural inhibitory substances (bactericides and/or bacteriostatics) are responsible for this hostile microenvironment.

The absence of moisture induces a state of dormancy in numerous residents of the microflora. However, on some body parts (the epicranium, the ears, the axillary regions, the

genitourinary and anal regions, the perineum and the palms) the moisture is sufficiently high to allow the existence of a resident microflora.

The acidic pH (4-6) of the skin, caused by the organic acids produced by the staphylococci and the secretions of the sebaceous and sudoriparous glands, discourages colonization by numerous microorganisms.

Perspiration contains sodium chloride at a concentration which establishes hyperosmotic conditions of the surface of the skin and has a negative osmotic effect on most of the microorganisms.

Finally, some natural inhibitory substances aid in controlling the colonization, the excessive growth and the infection of the surface of the skin by the resident microorganisms. For example, the sudoriparous glands excrete lysozyme which lyses *Staphylococcus epidermidis* and other Gram-positive bacteria.

Some Gram-positive bacteria (*Propionibacterium acnes*) can change the lipids which are secreted by the sebaceous glands into unsaturated fatty acids such as, for example, oleic acid, which have a strong antimicrobial activity on the Gram-negative bacteria and the mycetes.

However, under some conditions, this natural defense system can be effective but present annoyances, or it can even be defective.

For example, some natural inhibitory substances (bactericides and/or bacteriostatics) due to the partial degradation of the complex lipids secreted by the sudoriparous glands, are volatile and can be associated with a strong odor which one usually tries to fight. To be sure, numerous deodorants contain antibacterial substances which selectively act on the Gram-positive bacteria responsible for these degradations to reduce the production of aromatic unsaturated fatty acids and body odor. However, the deodorants can modify the microflora, primarily by promoting Gram-negative bacteria, and consequently it can trigger infections.

Thus, it remains of interest to be able to have available, in the context of the treatment of body odors, compounds and/or compositions which are effective while not presenting any side effects.

Another example is *Propionibacterium acnes*, the bacterium which is most frequently associated with the cutaneous glands and which is an anaerobic and lipophilic Gram-positive rod. This bacterium is usually inoffensive. However, it has been associated with a cutaneous disease, juvenile acne. Ordinarily, acne appears during adolescence when the endocrine system is very active. The hormonal activity stimulates the overproduction of sebum, a fluid which is secreted by the sebaceous glands. A large volume of sebum accumulates in the glands and provides an ideal microenvironment for *Propionibacterium acnes*. In some individuals, this accumulation triggers an inflammatory response which causes redness and a swelling of the glandular canal

and produces a comedo, a stopper of sebum and keratin in the canal. The result is inflammatory lesions (papula, pustules, nodules) which are commonly called "blackheads." *Propionibacterium acnes* seems to be the organism which produces lipases which degrade the triglycerides of the sebum into free fatty acids. These derivatives are particularly irritating because they can penetrate into the dermis and promote inflammation.

The yeasts *Pityrosporum ovale* and *Pityrosporum orbiculare* are commonly associated with the formation of dandruff.

The strains of *Staphylococcus aureus* are known to be super antigens, which promotes the appearance of irritation reactions and inflammatory processes.

Naturally, if necessary, it has been known for a long time to use compounds such as antibiotics or certain natural or synthetic derivatives of vitamin A to relieve the deficiencies of the natural defense system.

However, again, it is known that the use of such compounds presents non-negligible negative aspects. The abusive use of antibiotics can lead to the emergence of resistant microorganisms against which they are no longer effective. With regard to the derivatives of vitamin A, it is known that they generally present serious side effects, which makes their utilization delicate.

Thus, again, there is a need for compounds and/or compositions which are effective while presenting no side effects.

Moreover, it is known that one of the key elements for a pathogenic agent to induce an infectious disease is that it must be capable to adhere to the host which it will colonize and invade.

Indeed, after having been transmitted to an appropriate host, the pathogenic agent must be capable of attaching to the cells and the tissues of the host, and of colonizing them. The colonization depends on the capacity which the pathogenic microbe has to compete successfully with the normal microflora of the host for essential nutrients. Specialized structures which make it possible to compete for attachment sites on the surface are also necessary for the colonization.

The pathogenic organisms, like many nonpathogenes, attach in a very specific manner to particular tissues. These adherent structures are one of the elements of this specificity. They are specialized and present on the surface of the pathogenic agent, and they become attached to specific receptors of the host cells.

Thus, one can understand that one of the possible routes for treating the annoyances and/or the cutaneous infections is to fight against the adhesion of the microorganisms to the cells of the skin and/or the mucosal membranes.

Surprisingly and unexpectedly, the applicant has discovered that a mixture comprising Mn(II) and/or Zn(II) in combination with the bicarbonate and at least an ortho-diphenol presents the special property of modifying the attachment of the microorganisms to the cells, in particular to the cells of the skin and/or the mucosal membranes.

The invention thus concerns the utilization as active principle in or for the preparation of a composition of an effective quantity of at least one such mixture as defined above, where this mixture or the composition is intended to modify the adhesion of the microorganisms to the skin and/or the mucosal membranes.

The composition is preferably intended for cosmetic or dermatological, advantageously cosmetic, usage.

Active principle means any molecule or composition capable of modifying or modulating the function of at least one given biological system.

"Modify the adhesion of the microorganisms" means the capacity to prevent, completely or partially, the adhesion of the microorganisms, or the capacity as a curative to facilitate the detachment of the microorganisms.

Thus, the invention relates to the utilization as active principle in or for the preparation of a composition of an effective quantity of at least one mixture as defined above, where this mixture of the composition is intended to prevent, completely or partially, the adhesion of the microorganisms to the skin and/or the mucosal membranes.

Similarly, the invention relates to the utilization as active principle in or for the preparation of a composition of an effective quantity of at least one mixture as defined above, where this mixture or the composition is intended to facilitate the detachment of the microorganisms from the skin and/or the mucosal membranes.

In particular, the mixture or the composition containing it is used according to the invention for topical application to the skin and/or the mucosal membranes.

It has been seen above that the adhesion of microorganisms to the skin and/or the mucosal membranes has consequences ranging from simple annoyance (the odor) to diseases of various severity.

One of the aspects of the invention is thus to propose the utilization of at least one mixture as defined above as active principle in or for the preparation of a composition, where this mixture or the composition is intended for body hygiene care, including intimate care.

The expression body hygiene care refers to all the substances or preparations which are intended to come in contact with the different superficial parts of the human body and/or with the teeth and/or the mucosal membranes to clean them, to protect them, to maintain them in a good condition, to modify their appearance, to perfume them, or to correct their odor.

In particular, the invention relates to the utilization of at least one mixture as defined above as active principle in or for the preparation of a composition, where this mixture or the composition is intended to decrease the bad body odors.

It has been seen above that the bacterial flora of the surface of the skin is responsible for a large number of disorders.

Thus, the invention also relates to the utilization of at least one mixture as defined above as active principle in or for the preparation of a composition, where this mixture or the composition is intended to fight against mycoses, acne, particularly juvenile acne and/or dandruff.

In particular, the invention relates to the utilization of at least one mixture as defined above as an active principle in or for the preparation of a composition, where this mixture or the composition is intended to fight against acne and/or dandruff.

According to the invention, the molar concentration of Mn(II), Zn(II) or Mn(II) + Zn(II) in the final composition generally varies from 10^{-3} to 10 mM/L, preferably from 10^{-2} to 10 mM/L.

When one uses only Mn(II), the molar concentration of Mn(II) in the final composition is typically 10^{-3}-10^{1} mM/L, preferably 10^{-2}-10^{-1} mM/L.

It is preferred, when only Zn(II) is used, for the concentration of Zn(II) in the final composition to be 5×10^{-2} to 10 mM/L, or better 5×10^{-1} to 1 mM/L.

The Mn(II) and/or Zn(II) of the mixture generally originates from the a salt and/or an oxide of Mn(II) or Zn(II).

Among the salts of Mn(II) and Zn(II) which are suitable for the present invention, one can cite the compounds chloride, fluoride, iodide, sulfate, phosphate, nitrate and perchlorate, the salts of carboxylic acids and their mixtures.

As examples, one can cite manganese chloride, manganese carbonate (for example, rhodochrosite), Mn(II) difluoride, tetrahydrated Mn(II) acetate, trihydrated Mn(II) lactate, Mn(II) phosphate, tetrahydrated Mn(II) perchlorate and monohydrated Mn(II) sulfate.

The salts which are particularly preferred are $MnCl_2$ and $ZnCl_2$.

The salts of carboxylic acids also include hydroxylated salts of carboxylic acids, such as gluconate.

Generally, the bicarbonate originates from an alkali or alkaline earth bicarbonate.

Among the alkali and alkaline earth bicarbonates one can cite the bicarbonates of Na, K, Mg, Ca and their mixtures, preferably the bicarbonate of Na.

According to the invention, the molar concentrations of Mn(II), Zn(II) and HCO_3 in the mixture or the final composition are such that:

//insert, p. 8//

Key: 1 With
2 And

where [Mn(II)], [Zn(II)] and [HCO_3] represent the molar concentrations of Mn(II), Zn(II) and HCO_3, respectively, in the composition.

Generally, the ratio [Mn(II)]/[HCO_3] varies from 10^{-5} to 10^{-1}, preferably from 10^{-3} to 10^{-2}, and, typically, it is on the order of 5×10^{-3}.

In the case of Zn(II), the ratio [Zn(II)]/[HCO_3] is in general on the order of 10-100 times greater than the ratio in the case of Mn(II).

Typically, this ratio is 10^{-4} or more, preferably 10^{-3} or more, and preferably on the order of 5×10^{-1}.

In the case of a mixture of Mn(II) and Zn(II), the ratio generally varies from 10^{-5} to 10^{-1}, preferably 10^{-3} to 10^{-2}, where a higher value for this ratio is chosen when the proportion of Zn(II) in the mixture increases.

Generally, the molar concentration of Mn(II), Zn(II) or Mn(II) + Zn(II) in the final composition varies from 10^{-3} to 10 mM/L, preferably from 10^{-2} to 1 mM/L.

The ortho-diphenols of the mixtures of the invention can be represented by formula (I):

//insert formula (I), page 9//

in which the substituents R^1-R^4, which may be identical or different, represent a hydrogen atom, a halogen, hydroxyl, carboxyl, alkyl carboxylate radical, optionally substituted amino radical, optionally substituted linear or branched alkyl, optionally substituted linear or branched alkenyl, optionally substituted cycloalkyl, alkoxy, alkoxyalkyl, alkoxyaryl, where the aryl group can optionally be substituted, aryl, substituted aryl, and optionally substituted heterocyclic

radical, radical containing one or more silicon atoms, where two of the substituents R^1-R^4 together form a saturated or unsaturated ring optionally containing one or more heteroatoms and optionally condensed with one or more saturated or unsaturated rings optionally containing one or more heteroatoms.

The saturated or unsaturated, optionally condensed, rings can also optionally be substituted.

The alkyl radicals generally are the C_1-C_{10} alkyl radicals, preferably the C_1-C_6 alkyl radicals, such as methyl, ethyl, propyl, butyl, pentyl and hexyl.

The alkoxy radicals in general are the C_1-C_{20} alkoxy radicals, such as methoxy, ethoxy, propoxy and butoxy.

The alkoxy alkyl radicals preferably are the (C_1-C_{20}) alkoxy (C_1-C_{20}) alkyl radicals, such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, etc.

The cycloalkyl radicals in general are the C_4-C_8 cycloalkyl radicals, preferably the cyclopentyl and cyclohexyl radicals. The cycloalkyl radicals can be substituted cycloalkyl radicals, in particular those substituted by alkyl groups, alkoxy, carboxylic acid, hydroxyl, amine and ketone.

The alkenyl radicals are preferably C_1-C_{20} radicals such as ethylene, propylene, butylenes, pentylene, methyl-2-propylene and decylene.

The radicals containing one or more silicon atoms preferably are polydimethylsiloxane, polydiphenylsiloxane, polydimethylphenylsiloxane, and steraoxydimethicone radicals.

The heterocyclic radicals in general are radicals comprising one or more heteroatoms chosen from O, N and S, preferably O or N, optionally substituted by one or more alkyl groups, alkoxy, carboxylic acid, hydroxyl, amine or ketone.

Among the preferred heterocyclic radicals, one can cite the furyl, pyranyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, and thienyl radicals.

It is also preferred for the heterocyclic groups to be condensed groups such as benzofuranyl, chromenyl, xanthenyl, indolyl, isoindolyl, quinolyl, isoquinolyl, chromanyl, isochromanyl, indolinyl, isoindolinyl, coumarinyl, isocoumarinyl groups, where these groups can be substituted, in particular by one or more OH groups.

The preferred ortho-diphenols are:

- the flavanols such as catechin and epichatechin [sic; epicatechin] gallate,
- the flavonols such as quercetin,
- the anthocyanidins such as peonidin,
- the anthocyanins, for example, oenin,
- the hydroxybenzoates, for example, gallic acid,

- the flavones such as luteolin,
- the iridoids such as oleuropein,

where these products can be osylated (for example, glycosylated) and/or in the form of oligomers (procyanidins);

- the hydroxystilbenes, optionally osylated (for example, glycosylated), for example, 3,3',4,5'-tetrahydroxystilbene;
- 3,4-dihydroxyphenylalanine and its derivatives;
- 2,3-dihydroxyphenylalanine and its derivatives;
- 4,5-dihydroxyphenylalanine and its derivatives;

these derivatives can be of the L (L-DOPA) or D (D-DOPA) form,

- 4,5-dihydroxyindole and its derivatives;
- 5,6-dihydroxyindole and its derivatives;
- 6.7-dihydroxyindole and its derivatives;
- 2,3-dihydroxyindole and its derivatives;
- the dihydroxycinnamates such as caffeic acid and chlorogenic acid;
- the hydroxycoumarins;
- the hydroxyisocoumarins;
- the hydroxycoumarones;
- the hydroxyisocoumarones;
- the hydroxychalcones;
- the hydroxychromones;
- the anthocyans;
- the quinones;
- the hydroxyxanthones; and
- the mixtures thereof.

When the ortho-diphenols present D and L forms, the two forms can be used in the compositions according to the invention.

The ortho-diphenols can be extracts of plants, citrus fruit, legumes and mixtures of these extracts which contain numerous polyphenols as defined above.

Among the plant extracts, one can cite the extracts of rose and of tea.

Among the fruit extracts, one can cite the extracts of apple, grape (in particular grape seeds) and banana.

Among the legume extracts, one can cite the extract of potato [sic; not a legume].

One can also use mixtures of plant and/or fruit extracts, such as mixtures of extracts of apple and of tea and mixtures of extracts of grape and of apple.

The preferred ortho-diphenol is catechin.

The quantity of ortho-diphenol in the final composition can vary within broad ranges.

In general, the quantity of ortho-diphenol in the final composition is at least 10 μmol/mL of mixture or of final composition.

The compositions according to the invention can also contain an effective quantity of at least one amino acid comprising at least a thiol group (SH) and preferably a single thiol group, where these amino acids can be in the form of hydrochlorides.

The preferred amino acids according to the invention are the amino acids which contain an amine function in the α-position with respect to a carboxylic acid function.

The preferred amino acids can be represented by the formula (II):

//insert formula (II), page 12//

in which –R is a linear or branched divalent hydrocarbon radical, for example, a C_1-C_{10} hydrocarbon radical, preferably C_1-C_6, such as a methylene, ethylene, butylenes, ethylidene, propylidene radical, a divalent saturated cyclic radical, optionally substituted, for example, C_4-C_8, an optionally substituted divalent aromatic group such as a phenylene, tolylene, xylylene radical.

Among the preferred amino acids for the compositions according to the invention, one can cite cysteine and its derivatives, in particular L-cysteine and L-cysteine hydrochloride, and gluthatione [sic; glutathione] and its derivatives.

The relative proportions of amino acid and of oxidative dye precursor in the compositions of the invention can vary within broad ranges as a function of the desired coloration. In general, the molar ratio amino acid/dye precursor will vary from 0.001 to 50, preferably from 0.01 to 5, and more advantageously from 0.05 to 2.5.

In general, the content of amino acid with thiol group in the final composition is at least 0.01 μmol/mL, preferably at least 0.1 μmol/mL.

By varying the nature of the dye precursors and of the amino acids of the composition and the relative proportion of amino acid and dye precursor, one can obtain a palette of tints and in particular tints close to those of natural tanning.

Thus, the combination of cysteine and of dihydroxyindole allows the obtention of a chestnut brown hue closer to that of natural tanning than that obtained using dihydroxyindole alone, which only leads to a black color.

This combination makes it possible to achieve a natural coloration of the skin and of the hair which is a mixture of eumelanin and of phaeomelanin in variable proportions.

The constituents of the mixture according to the invention can be directly introduced into the composition, or they can be introduced in the form of solutions in a solvent or a mixture of appropriate solvents.

Among the solvents which are suitable for the mixture according to the invention, one can cite water, the alcohols, the polar solvents and their mixtures.

The alcohols preferably are lower (C_1-C_6) alkanols such as ethanol and isopropanol, and the alkanediols such as ethylene glycol, propylene glycol and pentanediol.

Among the polar solvents one can cite the ethers, the esters (in particular the acetates), dimethylsulfoxide (DMSO), N-methylpyrrolidone (NMP), the ketones (in particular acetone) and their mixtures.

The solvent preferably comprises water (in particular distilled or water treated with ion-exchange media) or a water/alcohol mixture, in particular water/ethanol.

The quantity of alcohol in the water/alcohol mixture can represent up to 80 wt% of the water/alcohol mixture, preferably 1-50 wt% and more advantageously 5-20 wt%.

The invention also relates to a cosmetic method to treat the disorders which are connected with the adhesion of the microorganisms, which method consists in applying to the skin a cosmetic composition comprising an effective quantity of a mixture according to the invention in a cosmetically acceptable medium.

Cosmetically acceptable medium means one which is compatible with the skin, the scalp, the mucosal membranes, the nails and the hair.

It can be in any of the galenic forms which are normally used for topical application, notably in the form of an aqueous, water-alcohol or oily solution, an oil-in-water or water-in-oil or multiple emulsion, an aqueous or oily gel, a liquid, pasty or solid anhydrous product, a dispersion of oil in an aqueous phase with the aid of spherules, where these spherules can be polymeric nanoparticles such as the nanospheres and the nanocapsules or more advantageously the lipid vesicles of the ionic and/or nonionic type.

This composition can be more or less fluid and it can have the appearance of a colored or white cream, an ointment, a milk, a lotion, a serum, a paste, and a foam. It can optionally be applied to the skin in the form of an aerosol. It can also be in a solid form and, for example, in the form of a stick. It can be used as a care product, as a cleaning product, as a makeup product or as a simple deodorant product.

Thus, the invention relates to a cosmetic care, cleaning, makeup or deodorant composition comprising a mixture according to the invention.

In particular, the invention relates to a deodorant cosmetic composition comprising a mixture according to the invention.

More specifically, the deodorant composition of the invention is in the form of a stick.

In the case where a coloration of the skin and/or the hair is not desirable, the composition will contain a formulation which prevents penetration into the stratum corneum or the hair fiber. One then preferably uses ortho-diphenols forming compounds which are slightly or not colored such as, for example, caffeic acid.

As is known, the composition of the invention can also contain the usual adjuvants in the cosmetic and dermatological fields, such as the hydrophilic or lipophilic gelling agents, hydrophilic or lipophilic active principles, preservatives, antioxidants, solvents, perfumes, fillers, filters, pigments, chelating agents, odor absorbing agents, dyes, matting agents and their mixtures. The quantities of these different adjuvants are those conventionally used in the fields considered, for example, 0.01-20 wt% of the total weight of the composition. These adjuvants, depending on their nature, can be introduced into the fatty phase, into the aqueous phase, into the lipid vesicles and/or into the nanoparticles.

When the composition of the invention is an emulsion, the proportion of the fatty phase can range from 5-80 wt%, and preferably from 5-50 wt% of the total weight of the composition. The oils, emulsifiers and coemulsifiers used in the composition in the form of an emulsion are chosen from those which are conventionally used in the field considered. The emulsifier and coemulsifier are present in the composition in a proportion from 0.3-30 wt%, and preferably 0.5-20 wt%, of the total weight of the composition.

As oils which can be used in the invention one can cite the mineral oils, the oils of plant origin (apricot oil, sunflower seed oil), the oils of animal origin, the synthetic oils, the silicone oils (cyclomethicone) and the fluorinated oils (perfluoropolyethers). One can also use, as fatty substances, fatty alcohols (cetyl alcohol), fatty acids, waxes (beeswax).

As emulsifiers and coemulsifiers which can be used in the invention, one can cite, for example, the esters of fatty acid and of polyethylene glycol, such as the stearate of PEG-40, the stearate of PEG-100, the esters of fatty acid and of polyol such as the stearate of glycerol and the tristearate of sorbitan.

As hydrophilic gelling agents, one can cite, in particular, the carboxyvinyl polymer (Carbomer), the acrylic copolymers such as the copolymers of acrylate/alkyl acrylates, the polyacrylamides, the polysaccharides, the natural gums and the clays, and, as lipophilic gelling agents, one can cite the modified clays such as the bentones, the metallic salts of fatty acids, hydrophobic silica and the polyethylenes.

As active principles, one can notably use hydrating agents such as the polyols (for example, glycerin), the vitamins (for example, D-panthenol), the anti-inflammatory agents, the smootheners (allantoin, cornflower water), the UVA and UVB filters, the matting agents (for example, the partially crosslinked polydimethylorganosiloxanes sold under the name KSG® by Shin Etsu), and their mixtures.

One can also add antiwrinkling active principles and notably stretching products such as plant proteins and their hydrolysates, in particular the soybean protein extract sold under the name Eleseryl® by the company LSN or the oats derivative sold under the name Reductine® by the Silab company.

The compositions according to the invention can be in various forms, such as in the form of liquids, creams, gels, or in any other appropriate form.

According to a first embodiment, the compositions according to the invention can be packaged in the form of an aerosol with single compartment containing all the ingredients of the composition and a conventional inert propellant such as nitrogen, a saturated hydrocarbon such as isopropane or a fluorinated hydrocarbon, for example, a Freon®.

In a second embodiment, the composition according to the invention can be packaged in the form of a kit comprising two distinct containers, one containing Mn(II) and/or Zn(II) and the ortho-diphenol, and optionally the amino acid(s), the other containing the bicarbonate, the content of the two compartments being mixed or successively applied at the time of use.

In a third embodiment, the composition can be contained in a pump system with single compartment, without air intake, or in a system with pump with two compartments, Mn(II) and/or Zn(II) and the ortho-diphenol being in one compartment and the bicarbonate in the other.

Other characteristics and advantages of the invention will be more apparent in the following examples and figures in the appendix, which are given as nonlimiting illustrations. The proportions are given in wt%.

Example 1

Measurement of the activity of a mixture according to the invention on the adhesion of microorganisms to the skin and on the human mucosal membranes

The activity of the mixture according to the invention on the adhesion of microorganisms to the skin or to the human skin or mucosal membranes is tested on a model of bacterial skin adhesion, as described below.

This ex vitro model of bacteria/skin adhesion is based on the use of explants of intact human skin mounted in a sandwich arrangement between a plate having 96 bottomless wells and a glass plate. Before the mounting, one eliminates the hypodermis from the skin and one freezes

the skin at -80°C. After thawing, the skin fragment is dialyzed in three baths of saline phosphate buffer (PSB [sic; PBS, phosphate-buffered saline]), at 4°C, for 3 h. The skin is mounted immediately before the test. To prevent drying, the entire experiment takes place with the skin immersed in a PBS bath.

50 µL of a diluted bacterial suspension of *Staphylococcus eperdermidis* [sic; epidermidis] (ATCC 12228) are distributed on the skin in sealed wells. After 2 h of incubation at 20°C, the wells are washed three times with saline phosphate buffer (PBS) to eliminate the nonadherent bacteria.

100 µL of the solutions below are distributed in the wells and one again incubates for 1 h at 20°C. The products and the free bacteria are then removed, and the wells are washed three times with PBS. The bacteria which are still adherent are detached from the skin with 100 µL of 4 M/L guanidine chaotropic buffer; 5 mM/L EDTA in 50 mM/L Tris-HCl, pH 8.0).

The solutions used had the following compositions:

1. 1 mM/L $MnCl_2$ solution in distilled water,
2. 100 mM/L $NaHCO_3$ solution in distilled water;
3. 100 mM/L catechin solution in ethanol;
4. Mixture according to the invention consisting of 180 µL of solution 1,180 µL of solution 2 and 40 µL of solution 3.

The positive control (guanidine) is also included in the study as reference.

20 µL of each sample of detached bacteria are transferred to nitrocellulose membranes with the aid of a "slot blot" matrix allowing subsequent densitometric quantification. The membranes are then saturated overnight at 4°C with a PBS/0.005% Tween (PBST) solution containing 1 wt% of skim milk. After washing in PBST, the bacteria are labeled with a streptavidin-peroxidase conjugate for 1 h at 20°C. After extensive washing, the immobilized biotins were developed by chemoluminescence on Kodak MP film. The acquisition of the images is then carried out on Gel Print 2000i and the densitometric measurements of the percentage of adherent bacteria are obtained with the aid of One-D-Scan software.

The results are given in Table I below.

Table 1

//insert Table I, page 18//

Key: 1 Control
2 Positive control (guanidine)
3 Solution 3
Catechin
4 Mixture 4
5 Adherent bacteria, %

Control: PBS buffer alone

Positive control: Guanidine 4 M/L guanidine; 5 mM/L EDTA in 50 mM/L Tris MCl [sic; HCl], pH 8.0—stimulates the desorption of the bacteria and inhibits adhesion.

The results show that while solution 1 (Mn) and solution 3 (catechin) appreciably reduce the adhesion of the bacteria, mixture 4 according to the invention containing the three active principles, Mn, HCO_3 and catechin, results in the complete disappearance of adhesion.

Claims

1. Use in or for the preparation of a composition as active principle of an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended to modify the adhesion of the microorganisms to the skin and/or the mucosal membranes.

2. Use in or for the preparation of a composition as active principle of an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended to prevent, entirely or partially, the adhesion of the microorganisms to the skin and/or the mucosal membranes.

3. Use in or for the preparation of a composition as active principle of an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended to facilitate the detachment of the microorganisms from the skin and/or the mucosal membranes.

4. Use according to any of the preceding claims, characterized by the fact that the mixture of the composition is used for topical application to the skin and/or the mucosal membranes.

5. Use in or for the preparation of a composition as active principle of an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended for body hygiene care.

6. Use in or for the preparation of a composition as active principle of an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended for intimate hygiene care.

7. Use in or for the preparation of a composition as active principle of an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended to decrease the bad odors.

8. Use in or for the preparation of a composition as active principle of an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended to fight against mycoses and/or acne and/or dandruff.

9. Use according to the preceding claim, characterized by the fact that the composition is intended to fight against juvenile acne.

10. Use according to any one of the preceding claims, characterized by the fact that the molar concentrations [Mn(II)], [Zn(II)] and [HCO_3] in the mixture or the final composition are such that:

//insert, pp. 20-21//

Key: 1 With
2 And

where [Mn(II)], [Zn(II)] and [HCO_3] represent the molar concentrations of Mn(II), Zn(II) and HCO_3, respectively, in the mixture or the composition.

11. Use according to Claim 10, characterized in that the ratio [Mn(II)]/[HCO_3] varies from 10^{-5} to 10^{-1}, preferably from 10^{-3} to 10^{-2}, and better it is on the order of 5×10^{-3}.

12. Use according to Claim 10 or 11, characterized in that the ratio [Zn(II)]/[HCO_3] is at least 10^{-4}, preferably at least 10^{-3}, and better it is on the order of 5×10^{-1}.

13. Use according to Claim 10, characterized in that the ratio [Mn(II) + Zn(II)]/[HCO_3] varies from 10^{-5} to 10^{-1}, preferably 10^{-3} to 10^{-2}.

14. Use according to any one of the preceding claims, characterized in that the ortho-diphenol is a compound having formula (I):

//insert formula (I), page 21//

in which the substituents R^1-R^4, which may be identical or different, represent a hydrogen atom, a halogen, hydroxyl, carboxyl, alkyl carboxylate radical, optionally substituted amino radical, optionally substituted linear or branched alkyl, optionally substituted linear or branched alkenyl, optionally substituted cycloalkyl, alkoxy, alkoxylalkyl, alkoxyaryl, where the aryl group can optionally be substituted, aryl, substituted aryl, and optionally substituted heterocyclic radical, radical containing one or more silicon atoms, where two of the substituents R^1-R^4 together form a saturated or unsaturated ring optionally containing one or more heteroatoms and optionally condensed with one or more saturated or unsaturated rings optionally containing one or more heteroatoms.

15. Use according to any one of Claims 1-13, characterized in that the ortho-diphenol is chosen from the flavanols, the flavonols, the anthocyaninidins, the anthocyanins, the hydroxybenzoates, the flavones, the iridoids, where these compounds can optionally be osylated and/or in the form of oligomers, the optionally osylated hydroxystilbenes, 3,4-dihydroxyphenylalanine and its derivatives, 2,3-dihydroxyphenylalanine and its derivatives, 4,5-dihydroxyphenylalanine and its derivatives, 4,5-dihydroxyindoles and its derivatives, 5,6-dihydroxyindole and its derivatives, 6,7-dihydroxyindole and its derivatives, 2,3-dihydroxyindoles and its derivatives, the dihydroxycinnamates, the hydroxycoumarins, the hydroxyisocoumarins, the hydroxycoumarones, the hydroxyisocoumarones, the hydroxychalcones, the hydroxychromones, the anthocyans, the quinines, the hydroxyxanthones, and the mixtures of two or more of the preceding compounds.

16. Use according to any one of Claims 1-3, characterized in that the ortho-diphenol is chosen from extracts of plants, fruit, citrus fruit, legumes and their mixtures.

17. Use according to Claim 16, characterized in that the ortho-diphenol is chosen from the extracts of tea, grape, apple, banana, potato and their mixtures.

18. Use according to any one of the preceding claims, characterized in that the ortho-diphenol is catechin.

19. Use according to any one of the preceding claims, characterized in that the ortho-diphenol is present in a quantity of at least 10 μmol/mL of mixture or composition.

20. Use according to any one of the preceding claims, characterized by the fact that the composition is in the form of a water-alcohol aqueous solution or an oil solution.

21. Use according to any one of Claims 1-15, characterized in that the composition is in the form of an oil-in-water or water-in-oil or multiple emulsion.

22. Use according to any one of Claims 1-15, characterized by the fact that the composition is in the form of an aqueous or oily gel.

23. Use according to any one of Claims 1-19, characterized by the fact that the composition is in the form of a liquid, a pasty or solid anhydrous product.

24. Use according to any one of Claims 1-19, characterized by the fact that the composition is in the form of a dispersion of oil in an aqueous phase with the aid of spherules.

25. Use according to any one of the preceding claims, characterized by the fact that the composition contains, in addition, at least an adjuvant chosen from the hydrophilic or lipophilic gelling agents, hydrophilic or lipophilic active principles, preservatives, antioxidants, solvents, perfumes, fillers, filters, pigments, chelating agents, odor absorbing agents, dyes, matting agents and their mixtures.

26. Method for cosmetic treatment to treat disorders connected with the adhesion of microorganisms, consisting in applying to the skin a cosmetic composition comprising at least a mixture of Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol in a cosmetically acceptable medium.

27. Deodorant cosmetic composition comprising an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with hydrogencarbonate and at least an ortho-diphenol, where this mixture or the composition is intended to modify the adhesion of the microorganisms to the skin and/or the mucosal membranes.

28. Deodorant stick comprising an effective quantity of a mixture comprising Mn(II) and/or Zn(II) in combination with bicarbonate and at least an ortho-diphenol, where this mixture or the composition is intended to modify the adhesion of the microorganisms to the skin and/or the mucosal membranes.

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